



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07D 295/22		A1	(11) International Publication Number: WO 96/36621 (43) International Publication Date: 21 November 1996 (21.11.96)
<p>(21) International Application Number: PCT/NL96/00201</p> <p>(22) International Filing Date: 14 May 1996 (14.05.96)</p> <p>(30) Priority Data: 1000396 18 May 1995 (18.05.95) NL</p> <p>(71) Applicant (for all designated States except US): COÖPERATIEVE VERKOOP- EN PRODUKTIEVERENIGING VAN AARDAPPELMEEL EN DERIVATEN AVEBE B.A. [NL/NL]; Beneden Oosterdiep 27, NL-9641 JA Veendam (NL).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): HEERES, Andre [NL/NL]; Taco Mesdagstraat 23a, NL-9718 KJ Groningen (NL). VAN DOREN, Hendrik, Arend [NL/NL]; Hanckemaborg 5, NL-9722 WD Groningen (NL). BLEEKER, Ido, Pieter [NL/NL]; Poldermolen 22, NL-9791 LS Ten Boer (NL). GOTLIEB, Cornelis, Fester [NL/NL]; Wildervankstraat 12, NL-9643 LC Veendam (NL).</p> <p>(74) Agent: SMULDERS, Th., A., H., J.; Vereenigde Octrooibureaux, Nieuwe Parklaan 97, NL-2587 BN The Hague (NL).</p>		<p>(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i></p>	
<p>(54) Title: METHOD FOR RECOVERING OR RECIRCULATING STABLE NITROXIDE RADICALS</p> <p>(57) Abstract</p> <p>The invention relates to a method for recovering stable nitroxide radicals, wherein at least a part of a reaction mixture consisting of a solution or suspension, or a filtrate or supernatant of a suspension, in which stable nitroxide radicals are present in non-solid form, is subjected to an azeotropic distillation. The invention further relates to a method for the selective oxidation of compounds which contain at least one hydroxyl group, using stable nitroxide radicals as catalyst, wherein the liquid phase of the mixture containing the reaction products is subjected to an azeotropic distillation, whereafter the nitroxide radical-containing distillate is recirculated to the reaction vessel.</p>			

FOR THE PURPOSES OF INFORMATION ONLY

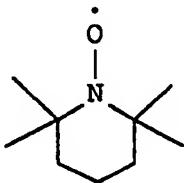
Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgyzstan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LI	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TG	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

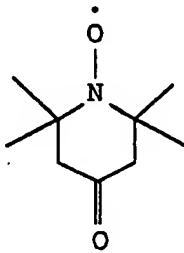
Title: Method for recovering or recirculating stable nitroxide radicals.

This invention relates to a method for substantially quantitatively recovering stable nitroxide radicals, in particular 2,2,6,6-tetramethylpiperidine-N-oxyl (TEMPO), from a reaction mixture, for the purpose of re-using them, 5 if desired in a continuous process.

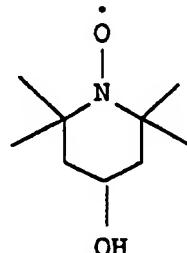
Stable nitroxide radicals, such as 2,2,6,6-tetramethylpiperidine-N-oxyl (TEMPO), 4,4-dimethyloxazolidine-N-oxyl (DOXYL) and 2,2,5,5-tetramethylpyrrolidine-N-oxyl (PROXYL), as well as derivatives thereof, are eminent catalysts for 10 the selective oxidation of hydroxyl group-containing compounds and especially compounds with a primary hydroxyl group. In the presence of these catalysts, primary hydroxyl groups present in compounds are converted, depending on the reaction conditions chosen, into aldehyde functionalities 15 and/or carboxyl groups. Secondary alcohols are oxidized to the corresponding ketones. Particularly TEMPO (see formula I), the TEMPO derivatives 4-oxo-2,2,6,6-tetramethylpiperidine-N-oxyl (OTEMPO; see formula II), 4-hydroxy-2,2,6,6-tetra-methylpiperidine-N-oxyl (TEMPOL; see 20 formula III) and other derivatives with a 2,2,6,6-tetramethylpiperidine-N-oxyl-(TEMPO)-skeleton are very suitable for use as catalyst for the selective oxidation of hydroxyl groups.



I



II



III

The catalysed reactions occur in the presence of an oxidizing agent, for instance sodium hypochlorite, sodium hypobromite, copper salts or nitric acid.

5 A method for the selective oxidation of primary hydroxyl group-containing compounds by the - *in situ* generated - oxammonium salt of TEMPO is for instance described in R. Siedlecka, J. Skarzewski and J. Mlochowski, *Tetrahedron Lett.*, 31 (1990) 2177-2180.

10 An overview of the possible applications of TEMPO and derivatives thereof in redox systems is given in M. Yamaguchi, T. Miyazawa, T. Takata and T. Endo, *Pure Appl. Chem.*, 62 (1990) 217-222.

15 Recently, it has been described that it is very well possible with the aid of stable nitroxide radicals to selectively oxidize the primary hydroxyl groups of carbohydrate derivatives substituted to the anomeric centre, to carboxyl groups. In this connection, reference is made to N.J. Davis and S.L. Flitsch, *Tetrahedron Lett.*, 34 (1993) 1181-1184; A.E.J. de Nooy, A.C. Besemer and H. van Bekkum, *Rec. Trav. Chim. Pays-Bas*, 113 (1994) 165-166; A.E.J. de Nooy, A.C. Besemer and H. van Bekkum, *Carbohydr. Res.* 269 (1995) 89-98 and Dutch patent application 9301549.

20 Stable nitroxide radicals, such as TEMPO, DOXYL and PROXYL, as well as derivatives thereof, can for instance be used as catalyst in the oxidation of carbohydrates in aqueous suspensions and solutions. During the isolation of the reaction product the catalyst is often lost or the catalyst remains present in the reaction product as an impurity. In view of the toxicity of the reactive nitroxide radicals and in particular of TEMPO (see T.S. Straub, *J. Chem. Educ.*, 68 (1991) 1048-1049) and from the point of view of cost price, this is an undesired situation. Accordingly, there is a need for a method for recovering these catalysts in a simple manner in order to be able to re-use these catalysts.

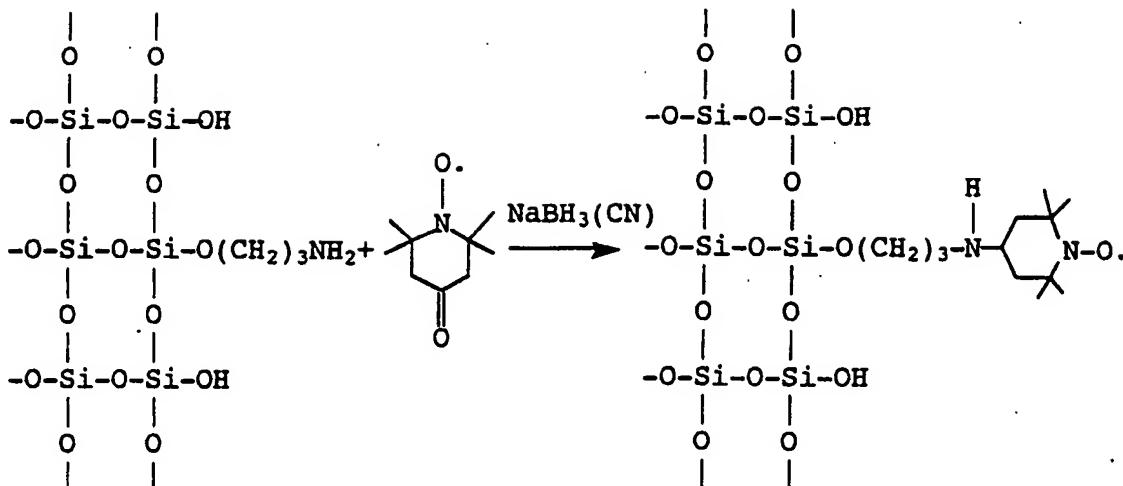
35 A possible method for this purpose has been described by T. Miyazawa, T. Endo and M. Okawara in *J. Polym. Sci.*,

5 Polym. Chem. Ed., 23 (1985) 1527-1535. In this article a radical (co)polymerization of a monomer which contains a TEMPO precursor is described. After the polymerization the TEMPO precursor fragments in the (co)polymer are converted to TEMPO fragments. Thus an immobilized catalyst in solid form is obtained, with which oxidation reactions can be catalysed. This catalyst can upon completion of the reaction be separated by means of filtration (T. Mizayawa and T. Endo, J. Polym. Sci., Polym. Chem. Ed., 23 (1985) 10 2487-2494).

15 German patent application 42.09.869 describes a method for immobilizing 4-hydroxy-TEMPO (TEMPOL; for instance available from Sigma-Aldrich) on polyvinyl -benzyl chloride, whereby likewise an active immobilized catalyst is obtained.

20 15 Further, the present inventors have found a different method for immobilizing TEMPO on a solid support. This method is represented in DIAGRAM I below. The method starts from the commercially available 4-oxo-TEMPO (OTEMPO; for instance available from Sigma-Aldrich) which through a 25 reductive amination reaction is coupled to silica gel modified with amino groups. The immobilized TEMPO thus obtained in a single-stage process has a catalytic activity in aqueous systems and can, with only a slight decrease in activity, be recovered and re-used. This method can be 25 carried out simply and rapidly.

- 4 -



However, the use of nitroxides such as TEMPO that are immobilized (on solid supports) is less successful in

5 reactions in which the compound to be oxidized is present in suspension or in which a homogeneous catalysis system offers advantages in other respects. The reaction rate is then much lower. If the product of a reaction in the presence of an (immobilized) solid catalyst is water-insoluble, this leads
10 to problems in the separation of the suspended product and the often toxic catalyst immobilized on a solid support.

The object of the present invention is to provide a method whereby stable nitroxide radicals which are present in non-solid form in a liquid reaction medium can be recovered from reaction mixtures and thereafter can be re-used. Such a method is suitable both for use during reactions that are carried out in a, preferably aqueous, solution, and for use during reactions that are carried out
15 in a, preferably aqueous, suspension.

20 It has presently been found that stable nitroxide radicals form azeotropes with liquids in which these radicals dissolve. These azeotropes possess substantially a catalytic activity which is of the same order as that of an amount of a solution that contains the same amount of fresh
25 nitroxide radicals.

Accordingly, the invention relates to a method for obtaining a catalytically active mixture based on stable nitroxide radicals, in which at least a part of a reaction mixture consisting of a solution or suspension, or a 5 filtrate or supernatant of a suspension, in which stable nitroxide radicals are present in non-solid form, is subjected to an azeotropic distillation. The stable nitroxide radicals are thereby at least partly distilled over with a part of the liquid medium.

10 It is noted that in the Soviet Russian patent publication SU-A-1 583 415 the production of 4-hydroxy-TEMPO is described. This radical is prepared by reacting 4-hydroxy-2,2,6,6-tetramethylpiperidine with hydrogen peroxide in a medium of aliphatic or cycloaliphatic 15 hydrocarbons, in particular in hexane and cyclohexane. It is stated that by distilling off an azeotrope of hexane or cyclohexane with water, the separation of the intended product is facilitated. The present inventors have reproduced the above and found that in the formation of the 20 azeotrope of hexane or cyclohexane with water, 4-hydroxy-TEMPO does not come over with the azeotrope.

In addition, it is known from European patent application 0 420 790 that 4-hydroxy-TEMPO can be used as polymerization inhibitor during the preparation of ester 25 derivatives of p-hydroxydiphenylamine. These diphenylamines are used as stabilizer in oxidizable organic materials.

In particular, the use of 4-hydroxy-TEMPO is illustrated in Examples 1-3 of that European patent application. Along with a number of other compounds, 30 4-hydroxy-TEMPO is introduced into the solvent methyl methacrylate. The reaction mixture obtained is heated and an azeotrope is distilled off. The present inventors have not been able to demonstrate any 4-hydroxy-TEMPO in the mixture distilled over.

35 It is further observed that according to EP-A-0 420 790 4-hydroxy-TEMPO is used in amounts that are a factor of 30 lower than the amount of stable nitroxide radical which is

preferably used as catalyst according to the present invention.

The azeotropic distillation according to the invention can be carried out at different pressures. Preferably, it

5 occurs under reduced pressure, because the loss of stable nitroxide radicals is then less and distillation can be carried out at lower temperatures, which better guarantees the stability of the nitroxide radicals. It is noted that an advantage of distilling at normal pressure is that less

10 solvent needs to be distilled over.

In a preferred embodiment of the method according to the invention, as stable nitroxide radical 2,2,6,6-tetramethyl-piperidine-N-oxyl is used.

The method concerns evaporating at least a part of a

15 solution or suspension, or of a filtrate or supernatant of a suspension, in which a reaction catalysed by stable nitroxide radicals has occurred. In the evaporation the stable nitroxide radical forms an azeotropic mixture with an amount of the reaction medium. Thus the stable nitroxide

20 radical can be quantitatively recovered and reused.

The solution or the suspension in which the reaction is carried out which is catalysed by the stable nitroxide radicals preferably contains water. In that case, in accordance with the invention, an azeotrope of the nitroxide

25 radical with water is distilled over.

Optionally, the azeotropic distillate obtained according to the invention can be subjected to an extraction. The azeotropic distillation is then followed by an extraction of the obtained solution with a suitable

30 solvent, which is typically organic. The stable nitroxide radical which dissolves in the solvent can subsequently be recovered from this solvent in a known manner.

The invention further relates to a method for recirculating stable nitroxide radicals in a continuous

35 process, in which the liquid phase of the product stream (the mixture which contains the reaction products) is subjected to an azeotropic distillation, whereafter the

nitroxide radical-containing distillate is returned to the reaction vessel.

In a preferred embodiment, this method involves the selective oxidation of compounds which contain at least one hydroxyl group, using stable nitroxide radicals as catalyst, in which the liquid phase of the mixture which contains the reaction products is subjected to an azeotropic distillation, whereafter the nitroxide radical-containing distillate is recirculated to the reaction vessel. Examples of such compounds to be oxidized are polysaccharides such as starch, cellulose and inulin, as well as derivatives thereof, and lower carbohydrates where the C₁-position is protected against oxidation, for instance by the presence of substituents or 1,4-compounds. These catalysed reactions occur in the presence of an oxidizing agent, for instance sodium hypochlorite, sodium hypobromite, copper salts or nitric acid.

Preferably, this oxidation reaction is carried out in an aqueous solution or aqueous suspension.

In a characteristic embodiment of this method, a primary hydroxyl group-containing compound is dissolved or suspended in a suitable medium, for instance water. In this medium, a catalytic amount of stable nitroxide radical, preferably TEMPO, has been added. Then, at a constant pH and at a temperature of about -10°C to 100°C, preferably of -5°C to 20°C, under stirring an oxidizing agent is added dropwise or batchwise.

The desired pH depends on the oxidizing agent used. When sodium hypochlorite in water is used as oxidizing agent, the pH is as a rule between about 6 and 13, and preferably between 8 and 10. If as oxidizing agent sodium hypochlorite in the presence of a little sodium bromide is employed, the pH is preferably 9-11.5. The pH is maintained constant by dripping a base or a solution thereof in water, for instance a 1M sodium or potassium hydroxide solution or an aqueous solution of sodium hydrogen carbonate, to the

reaction mixture. The reaction has gone to completion if no consumption of base occurs anymore.

When only a partial oxidation is desired, this can be effected by adding less hypochlorite and/or by quenching the 5 reaction with, for instance, methanol or ethanol.

Thereafter the reaction mixture, after optional decanting, centrifugation or filtration, is transferred into a vessel, for instance a flask, which is suitable for distillation under reduced pressure. The flask is placed in 10 a heatable water bath and the pressure is reduced, for instance using a vacuum pump on a rotary evaporator, to the point where water begins to distill over. As soon as the pressure has been reduced sufficiently, the system is closed off to prevent loss of material via the vacuum pump. The 15 catalyst, in particular TEMPO, is found to be azeotropically distilled over with the first amount of water. Therefore, the catalytically active material can be quantitatively removed from the reaction mixture.

The catalyst recovered in this manner, dissolved in 20 water or any other azeotrope-forming liquid reaction medium, can be reused. No reduction of the activity of the catalyst arises.

It is possible to recover the stable nitroxide radical, for instance TEMPO, in solid form by extraction of the 25 distilled-over, preferably aqueous, azeotrope with a suitable solvent, for instance an organic solvent such as diethyl ether, followed by drying of the fraction comprising this solvent and evaporation to dryness. This resultant material has been found to have substantially the same 30 catalytic activity as the starting material.

It is noted that it is by no means necessary to have the distillation occur under reduced pressure. Distillation at atmospheric pressure is equally satisfactory when a sufficiently efficient cooling of the distillate is used.

35 The invention further relates to the use of stable nitroxide radicals in the form of a distillate which has

been obtained from an azeotropic distillation or an extract from this distillate as catalyst.

Using the method according to the invention, it is possible to have the selective oxidation of hydroxyl group-containing compounds take place continuously. A compound to be oxidized can be fed to a reaction vessel in a suitable medium with simultaneous discharge of a product stream. The product stream can optionally be subjected to a separation step in which solid substances are separated from the liquid medium. This liquid medium is then distilled, whereby an azeotrope with all catalytic activity therein is formed. This azeotrope can then be returned to the reaction vessel.

The invention is presently further illustrated in and by a few non-limiting examples. Other stable nitroxide radicals which form an azeotrope with water or other solvents can also be used. The permanent activity of the recovered catalyst is shown in Table 1.

Example 1

20 Recovery of TEMPO through azeotropic distillation

In a 100 ml flask 0.50 g TEMPO (3.2 mmol) was dissolved in 60 ml water. The flask was provided with a distillation set-up, to which an efficient cooler and a collecting flask were connected. Under stirring, the solution was heated to a boil. An azeotropic mixture of TEMPO and water was distilled over until the residual liquid became colourless. Thus 10 ml distillate was obtained.

The distilled-over TEMPO containing water fraction was thereupon extracted with 2 x 15 ml diethyl ether. The ether fractions were put together and dried with sodium sulfate. After filtration, the ether was evaporated on a rotary film evaporator.

Yield: 0.45 g slowly crystallizing TEMPO (m.p. = 33-36°C). Because the distillation occurred in a non-

closed system, a small part of the catalyst was lost through evaporation.

Example 2 -

Recovery of TEMPO through azeotropic distillation under 5 reduced pressure

In a 500 ml flask 0.50 g TEMPO (3.2 mmol) was dissolved in 250 ml H₂O. Using a rotary evaporator, under reduced pressure a water fraction of 60 ml was distilled over until the residual liquid became colourless. The TEMPO-containing 10 water fraction distilled over under reduced pressure was extracted with 2 x 50 ml ether. The ether fractions were dried with sodium sulfate and after filtration the ether was evaporated on the film evaporator.

Yield: 0.49 g slowly crystallizing TEMPO 15 (m.p. = 35-37°C).

Example 3

Oxidation of starch with regenerated TEMPO

3(a): 1.92 g Starch (native potato starch, AVEBE; d.s. (dry substance content) = 86.90%, 10.3 mmol) was suspended 20 in 20 ml water which contained 0.06 g TEMPO (0.38 mmol) and 0.21 g NaBr (2.0 mmol). With an aqueous 1 M KOH solution the pH of the suspension was adjusted to 10.8. At a temperature of 0°C, 10.3 ml NaOCl solution (150 g/l, ± 21.1 mmol) was gently added dropwise to the suspension in a time interval 25 of 30 minutes. By additions of a 1 M KOH solution (in total 11.53 ml) the pH was meanwhile maintained at a constant value of 10.8. After 30 minutes' stirring, after which the pH was found to have become virtually constant, the solution was neutralized to pH = 7 by addition of a 0.5 N HCl 30 solution.

The solution was distilled in a fully closed rotary evaporator under reduced pressure until 20 ml distillate had been collected. In this manner the TEMPO present in the reaction mixture was quantitatively distilled over.

The fraction which contained the polyglucuronic acid formed in the reaction was poured out into 100 ml ethanol, filtered, washed with a 70 % ethanol solution and dried in air.

5 Yield: 2.30 g polyglucuronic acid, d.s. = 81.10%
3(b): To the TEMPO containing distillate were added 1.92 g starch (d.s. = 86.9%, 10.3 mmol) and 0.20 g NaBr (1.94 mmol). At a temperature of 0°C, 10.3 ml NaOCl solution (150 g/l, \pm 21.1 mmol) was carefully dripped into this
10 suspension over a time interval of 30 minutes. By additions of a 1 M KOH solution (in total 11.67 ml) the pH was maintained at a constant value of 10.8. After 30 minutes' stirring, whereafter the pH was virtually constant, the solution was neutralised to pH = 7 by addition of a 0.5 N HCl solution. The solution was distilled in a fully closed rotary evaporator under reduced pressure until 20 ml
15 distillate had been collected. In this manner the TEMPO present in the reaction mixture was quantitatively distilled over. The polyglucuronic acid-containing fraction was poured
20 out into 100 ml ethanol, filtered, washed with a 70% ethanol solution and then with acetone and dried in air.

Yield: 1.97 g polyglucuronic acid, d.s. = 83.87%.

3(c): Then the distillate obtained in 3(b) was used in conformity with the procedure of 3(b), instead of the
25 distillate obtained under 3(a).

Yield: 2.38 g polyglucuronic acid, d.s. = 82.19%.

The results of the methods according to Examples 3(a)-(c) are schematically summarised in Table 1.

Table 1
 Use of regenerated TEMPO
 for the oxidation of starch

Example no./ Amount of starch	Yield Potassium polyglucuronate	ds ¹ (in %)	Carboxyl content ² (meq.g ⁻¹)
3a 1.92 g (10.3 mmol)	2.30 g	81.10	4.1
3b 1.92 g (10.3 mmol)	1.97 g	83.87	4.5
3c 1.92 g (10.3 mmol)	2.38 g	82.19	4.7

5

¹ dry substance content

² reaction time not entirely constant; this explains the apparent increase in activity after regeneration.

10

Thus it has been demonstrated that the azeotropically recovered TEMPO maintains its catalytic activity.

CLAIMS

1. A method for obtaining a catalytically active mixture based on stable nitroxide radicals, wherein at least a part of a reaction mixture consisting of a solution or suspension, or a filtrate or supernatant of a suspension, in which stable nitroxide radicals are present in non-solid form, is subjected to an azeotropic distillation.
- 5 2. A method according to claim 1, wherein the azeotropic distillation occurs under reduced pressure.
3. A method according to claim 1 or 2, wherein as stable nitroxide radical 2,2,6,6-tetramethylpiperidine-N-oxyl is used.
- 10 4. A method according to any one of the preceding claims, wherein an azeotrope of the nitroxide radical with water is distilled over.
- 15 5. A method according to any one of the preceding claims, wherein the azeotropic distillation is followed by an extraction of the obtained solution with a suitable solvent, and the stable nitroxide radical is recovered from this solvent in a known manner.
- 20 6. A method for recirculating stable nitroxide radicals in a continuous process, wherein the liquid phase of the product stream is subjected to an azeotropic distillation, whereafter the nitroxide radical-containing distillate is recirculated to the reaction vessel.
- 25 7. A method according to claim 6, wherein the continuous process comprises selectively oxidizing compounds which contain at least one hydroxyl group, using stable nitroxide radicals as catalyst.
- 30 8. A method according to claim 6 or 7, wherein TEMPO is used as nitroxide radical.
9. A method according to any one of claims 6-8, wherein the oxidation reaction is carried out in an aqueous solution or aqueous suspension.

- 14 -

10. Use of stable nitroxide radicals in the form of a distillate which has been obtained from an azeotropic distillation or an extract from this distillate as catalyst.

INTERNATIONAL SEARCH REPORT

Int'l. Application No
PCT/NL 96/00201A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D295/22

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP,A,0 420 790 (GOODYEAR TIRE & RUBBER) 3 April 1991 see page 6, line 37 - line 43 see page 7, line 7 - line 15 see page 7, line 31 - line 38 ---	1-10
X	DATABASE WPI Section Ch, Week 9124 Derwent Publications Ltd., London, GB; Class A60, AN 91-176790 XP002008481 & SU,A,1 583 415 (POPOVA E G) , 7 August 1990 see abstract ---	1-10
A	GB,A,1 199 351 (BP CHEMICALS) 22 July 1970 ---	1 -/-

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

1

Date of the actual completion of the international search	Date of mailing of the international search report
16 July 1996	25.07.96
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Authorized officer Pauwels, G

INTERNATIONAL SEARCH REPORT

International Application No
PCT/NL 96/00201

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 104, no. 11, WASHINGTON DC US, pages 2951-2956, XP002008480 T. KAWAI ET AL.: "Hydrogenation of Nitroxides on Pt/SiO ₂ " see page 2952, paragraph 3 -----	1

INTERNATIONAL SEARCH REPORT

International Application No

PCT/NL 96/00201

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP-A-0420790	03-04-91	CA-A-	2019062	25-03-91
		JP-A-	3152163	28-06-91
		US-A-	5155148	13-10-92
GB-A-1199351	22-07-70	NONE		